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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,630	06/27/2003	Zeina Tannous	MGH-036AUS	8743

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SUITE 301A
354A TURNPIKE STREET
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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,630	TANNOUS ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/27/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Tannous et al.

1. The information disclosure statement (IDS) filed on 6/27/2003 has been considered. A signed copy is attached hereto.

2. Claims 1-11 are currently pending and under examination.

Drawings

3. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Fig. 5A and Fig. 5B. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Richards-Kortum et al. (US Patent No. 6,187,289 B1, Date of Patent 2/13/2001, effective filing date 10/20/1998).

Claims 1 and 10 is drawn to a method of enhancing optical characteristics of at least one cell anomaly associated with a tumor, comprising: (a) applying a predetermined contrasting solution to an *in-vivo* defect area associated with the tumor for optically enhancing the at least one cell anomaly associated with the tumor; and (b) imaging at least a portion of the *in-vivo* defect area associated with the tumor using a first optical imaging system to provide an *in-vivo* enhanced tumor image, wherein the in-vivo enhanced tumor image includes the at least one cell anomaly having enhanced attributes. The method is further limited wherein imaging using the first optical imaging system includes imaging using a confocal microscope.

Richards-Kortum et al. teach a method of using acetic acid as a contrast agent for confocal imaging of cells *in vivo* comprising the steps of (a) applying acetic acid to a diagnostic tissue sample in sufficient concentration to induce an alteration of the index of refraction of nuclei in the cells; and (b) imaging the cells using a reflectance confocal imaging system (see claims 1 and 4). Richards-Kortum et al. teach that after the addition of acetic acid, images of tissue can be obtained which illustrate characteristic differences between normal and neoplastic tissue throughout the entire epithelial thickness (see column 4, lines 31-41).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1 and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richards-Kortum et al. (US Patent No. 6,187,289 B1, Date of Patent 2/13/2001, effective filing date 10/20/1998) in view of Rajadhyaksha et al. (J. Invest. Dermatol. 1999, 113: 293-303).

The interpretations of claims 1 and 10 are set forth above (see paragraph 5).

Claims 5-9 and 11 embodies claim 1, the method further including step (c) freezing an excised predetermined layer of the in-vivo defect area associated with the tumor, step (d) imaging the excised predetermined layer of the in-vivo defect area associated with the tumor using a second predetermined optical imaging system to provide an ex-vivo enhanced tumor image, step (e) comparing the in-vivo enhanced tumor image and the ex-vivo tumor image to investigate the presence of the at least one cell anomaly, the method further includes: after step (a) applying sterile water to the in-vivo defect area for further optically enhancing the at least one cell anomaly, after step (a) applying an optically transparent sterile tape to the in-vivo defect area for sterilizing the in-vivo defect area, imaging using the second predetermined optical imaging system includes imaging using a microscope.

The teachings of Richards-Kortum et al. are set forth above as they apply to claims 1 and 10 (see paragraph 5 above).

Richards-Kortum et al. do not teach using sterile water and optically transparent sterile tape. Richards-Kortum et al. do not teach freezing and imaging an excised predetermined layer of the *in-vivo* defect area associated with tumor using a microscopy and comparing the *in vivo* tumor image with ex-vivo tumor image. However, these teachings are made up for in the teachings of Rajadhyaksha et al.

Rajadhyaksha et al. teach a method of *in vivo* imaging of human normal and abnormal skin using confocal scanning laser microscopy (see abstract, left column, lines 406) and comparison with histology (see page 299, left column, lower section) and confocal images of hematoxylin and eosin-stained skin (see page 300, left column). Rajadhyaksha et al. teach using water or cane-sugar solutions as immersion media to further enhance the contrast (see page 294, 2nd paragraph, lines 32-34, and 3rd paragraph, last sentence). Further Rajadhyaksha et al. teach using medical-grade adhesive tape to attach the ring and template to skin (see page 295, under skin-contact device).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include sterile water and tape in the method of Richards-Kortum et al. and further comparing the in vivo image with ex-vivo image in view of the teachings of Rajadhyaksha. One would have been motivated to include sterile water and tape in the method of Richards-Kortum et al. and further comparing the in vivo image with ex-vivo image because Rajadhyaksha et al. teach that specific

features are better delineated in the histology sections than *in vivo* and *ex-vivo* images provides additional insight into the interpretation of *in-vivo* confocal image (see page 300, 1st paragraph, lines 6-11), water can further enhance the image contrast and tape can be used to attach the ring and template to skin. While Rajadhyaksha et al. do not disclose the tape is for sterilizing the tissue, the medical grade tape used by Rajadhyaksha would inherently sterilize the tissues when it is applied to the skin. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to include sterile water and tape in the method of Richards-Kortum et al. and further comparing the *in vivo* image with *ex-vivo* image because Richards-Kortum et al. teaches the method of *in vivo* tumor imaging using a contrasting solution, Rajadhyaksha et al. teach a method of *in vivo* imaging using confocal microscopy and comparison of *in vivo* image with *ex-vivo* image.

8. Claims 1, 2-4 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richards-Kortum et al. (US Patent No. 6,187,289 B1, Date of Patent 2/13/2001, effective filing date 10/20/1998) in view of Yamamoto (US Patent No. 4,395,398), Prevendar (US Patent No. 6,652,840, effective filing date at least 2/8/2002) and Klaveness et al. (US Patent No. 6,159,445).

The interpretations of claims 1 and 10 are set forth above (see paragraph 5).

Claims 2-4 embodies claim 1, wherein applying the predetermined contrasting solution to the in-vivo defect area includes applying an AlCl solution having a predetermined concentration of Al and a predetermined concentration of Cl, applying

the AlCl solution includes applying an AlCl solution having a concentration ranging from approximately 20% to approximately 40%, and applying the predetermined contrasting solution to the in-vivo defect area includes applying a solution of AlCl (hexahydrate) 20% w/v in anhydrous ethyl alcohol (S.D. alcohol 40) 93% v/v.

The teachings of Richards-Kortum et al. are set forth above as they apply to claims 1 and 10 (see paragraph 5 above).

Richards-Kortum et al. do not teach using 20-40% AlCl solution. Richards-Kortum et al. do not teach using a solution of AlCl 20% in anhydrous ethyl alcohol. However, these deficiencies are made up for in the teachings of Yamamoto, Prevendar and Klaveness.

Yamamoto teaches that an aqueous solution containing 10-40 w/v% of aluminum chloride can be used as a hemostatic composition for local application to small hemorrhages in the dental field, for example, bleeding from gums which occurs during dental surgery (see column 1, lines 8-16 and 67-68). Yamamoto teaches a hemostatic solution of 25% AlCl in 20% ethanol and 50% ethanol (see Examples 6 and 7).

Prevendar teaches that an aqueous solution of aluminum chloride can also be used to stop bleeding and seal open small blood vessels while accelerating the healing process of skin (epithelial) tissues (see column 2, lines 29-31).

Klaveness teaches the use of particulate materials as contrast agents in *in vivo* light imaging including confocal microscopy (see abstract and column 8, line 48). Tumor can be imaged using said method (see column 18, line 63). Klaveness teaches unlike all the light imaging dyes or contrast agents described in the state of the art that

enhance contrast by changing the incident light absorption and/or fluorescence, the particulate materials enhance contrast by changing light scattering (see column 7, lines 49-65).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include 20%-40% AlCl solution, or a solution of 20% AlCl in anhydrous alcohol in the method of Richards-Kortum et al. in view of the teachings of Yamamoto, Prevendar and Klaveness. One would have been motivated to include 20%-40% AlCl solution, or a solution of 20% AlCl in anhydrous alcohol in the method of Richards-Kortum et al. because AlCl solution provides two advantages as taught by Yamamoto, Prevendar and Klaveness. The first advantage of using AlCl solution is that aluminum solution can be used to stop bleeding during and/or after surgery. Because the method of Rajadhyaksha et al. involves excising a layer of tissue for ex-vivo imaging, one would be motivated to use AlCl solution to stop tissue bleeding caused by excising the tissue. The second advantage of using AlCl solution is that AlCl when prepared in anhydrous alcohol forms fine particles that can change light scattering and enhance the contrast of image. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to include 20%-40% AlCl solution, or a solution of 20% AlCl in anhydrous alcohol in the method of Richards-Kortum et al. because Richards-Kortum et al. teaches the method of *in vivo* tumor imaging using a contrasting solution, and AlCl solution has been used in clinical practice for stopping bleeding.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit: 1643
Jan. 18, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER